REMARKS/ARGUMENTS

Claims 1, 2, 4, 5, 7 and 9-12 are now pending in the application. Claims 1, 7 and 9 are amended herein. Claim 8 is canceled herein having been incorporated into Claim 1.

Support for the amendment of Claim 1 to "having at least 75% sequence identity" and "forming a population of polynucleotides containing sequence variants, and at least 44% of the population has undergone reassortment of sequence information and the sequence variants have an average of 1 or more crossovers per 95 basepairs of heteroduplex polynucleotide sequence" is found at least in Examples 10 and 15 and in the attached Padgett Declaration 3.

Support for the amendments to Claim 7 is found at least in Example 15 and in the attached Padgett Declaration 3.

Support for the amendment of Claim 9 to "wherein at least 20% of the population has undergone reassortment of sequence information and the sequence variants have an average of 1 or more crossovers per 250 basepairs of heteroduplex polynucleotide sequence" is found at least in Example 15 and in the attached Padgett Declaration 3.

A Declaration from inventor Hal S. Padgett, Ph.D. is attached.

An Information Disclosure Statement is attached listing articles cited in co-pending related applications. Applicants submit that the cited references taken alone or in combination neither anticipate nor render obvious the present invention. Consideration of the foregoing in relation to this application is respectfully requested.

DETAILED ACTION

Item 2: Applicants acknowledge the withdrawal of rejections under 35 U.S.C. 103(a) over Arnold et al. in view of Mashal.

Claim Rejections - 35 U.S.C §112

Item 3: Claims 1-2, 4-5, and 7-12 were rejected under 35 U.S.C. 112, second paragraph as indefinite over the phrase "cleaving … with an effective amount of mismatch directed strand cleavage activity". The Examiner asserts "one cleaves with an enzyme having mismatch directed strand cleavage activity". Applicants point out the definition of "strand cleavage activity" in paragraph [0094] in which a variety of non-enzymatic agents can cause cleavage. Nevertheless, in order to advance prosecution of this application, the claims have been amended to clarify "cleaving … with an effective amount of an endonuclease having mismatch-directed strand cleavage activity". According, it is respectfully requested that this rejection be withdrawn.

Claim Rejections - 35 U.S.C § 103(a)

Items 4-5:

Claims 1, 4-5, and 7-8 were rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Shuber in view of Oleykowski. This rejection is respectfully traversed insofar as it might be applied to the amended claims.

Shuber presents a method for determining the DNA sequence at sites of mismatch in a heteroduplex. Shuber does not teach a method for reassortment of sequence information, or a method for generating a population of sequence variants as in the present invention. The method of Shuber utilizes dideoxynucleotides to determine the DNA sequences adjacent to, and including, the mismatch region. The use of dideoxynucleotides results in the termination of polynucleotide chain elongation. The use of dideoxynucleotides is therefore inappropriate for the instant method as the object of the instant method is to generate reassorted polynucleotides, not to generate fragments. One of skill in the art would not be motivated to substitute normal deoxynucleotides into the method of Shuber, because such a substitution would be expected to result in an inoperative invention, i.e., no DNA sequence would be determined. The addition of the teaching of Oleykowski et al. to the DNA sequence determination method of Shuber (i.e., substitution of CEL I into the method) merely results in another alternative mismatch recognition and cleavage system in addition to those listed in columns 7 and 8 of Shuber. The addition of CEL I into the method of Shuber does not result in the instant method.

In addition, Shuber makes no teaching and gives no guidance as to how one might form a population of polynucleotides containing sequence variants, with at least 44% of the population having undergone reassortment of sequence information and the sequence variants having an average of 1 or more crossovers per 95 basepairs of heteroduplex polynucleotide sequence as in the instant invention. Likewise, Shuber makes no teaching and gives no guidance as to how one might form a population of variants wherein at least 20% of the population has undergone reassortment of sequence information and the sequence variants have an average of 1 or more crossovers per 250 basepairs of heteroduplex polynucleotide sequence. As the cited references, alone or in combination, do not teach or suggest the claimed method, reconsideration and withdrawal of the rejection is respectfully requested.

Item 6.

Claims 2 and 9-12 were rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Shuber and Oleykowski and in further view of Arnold. This rejection is respectfully traversed insofar as it might be applied to the amended claims.

The failure of Shuber and Oleykowski to teach or suggest the currently claimed method is discussed above. Arnold is cited as teaching the formation of circular heteroduplexes and screening or selecting a population of variants. Arnold does not compensate for the deficiencies of Shuber and Oleykowski noted above. As the cited references, alone or in combination, do not teach or suggest the claimed method, reconsideration and withdrawal of the rejection is respectfully requested.

In view of the current claim amendments, declaration, and comments above, the rejections have been overcome. Reconsideration, withdrawal of the rejections and early indication of allowance are respectfully requested. If any issues remain, the Examiner is encouraged to call the undersigned for prompt resolution.

Applicants petition for an extension of time under the provisions of 37 CFR 1.136(a) for sufficient time to accept this response. The Commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.504391.

Respectfully submitted,

Date: November 24, 2008

/Wayne Fitzmaurice/
Wayne P. Fitzmaurice
Reg. No. 58,274

Enclosures:
- Padgett Declaration 3
- Information Disclosure Statement
- Petition for a one-month Extension of Time

Wayne P. Fitzmaurice
Novici Biotech LLC
3333 Vaca Valley Parkway, Suite 400
Vacaville, CA 95688
Tel.: (707) 446-5595
FAX.: (707) 446-3917
E-MAIL wayne.fitzmaurice@novicibiotech.com